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10/583,977	06/22/2006	Stefan Johan Koppelman	677132000200	8397

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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,977	KOPPELMAN ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/22/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-15 are pending.

2. Applicant's election of Group I, claims 1-13, in the reply filed on 10/01/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 14-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/01/2009.

4. Claims 1-13 are currently under consideration as they read on a method for treating an individual suffering from or having a tendency to develop a food allergy comprising administering to said individual a therapeutically effective amount of a modified food allergen, wherein the food allergen is modified by reduction and alkylation.

5. Applicant's IDS document filed on 08/22/2006 is acknowledged. The International Search report has been considered, but it has been crossed off because it has no publication date.

Claim Objections

6. Claims 5 and 8 are objected to because of the following informalities:

Claim 5 recites that the plant storage protein "is a tree nut." However, a plant storage protein cannot be a tree nut.

Claim 8 recites "N-ethylmalimide" but should recite "N-ethylmal**e**imide."

Appropriate correction is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-13 *are* rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of decreasing the allergenicity of 2S albumin Ber e 1 from brazil nuts by alkylating and reducing the protein, the specification does not provide reasonable enablement for: **a method for treating an individual suffering from or having a tendency to develop a food allergy** comprising administering to said individual a therapeutically effective amount of **a modified food allergen**, wherein **the food allergen** is modified by reduction and alkylation of claim 1; wherein **the food allergen** is **an allergenic food protein** of claim 2; wherein **the food allergen** is **a seed plant storage protein** of claim 3; wherein **the plant storage protein** is **a 2S albumin, lipid transfer protein (LTP), or conglutin** of claim 4; the **plant storage protein** is **a tree nut or a 2S albumin** of claim 5; wherein **the plant storage protein** is **brazil nut 2S albumin** of claim 6; **wherein said administering is in a dosage form chosen selected from the group consisting of a capsule, tablet, lozenge, dragee, pill,**

droplets, suppository, aerosol, powder, spray, vaccine, ointment, paste, cream, inhalant, or and patch of claim 9; **wherein said administering is effected orally, intraperitoneally, subcutaneously, intravenously, intramuscularly, pulmonarily, or via mucosa** of claim 11; **wherein administering the modified food allergen induces production of Thelper-1 mediated subclasses of IgG antibodies** of claim 12; and **wherein administering the modified food allergen results in down regulating the production of IgE antibodies** of claim 13 and as applied to claims 7-8 and 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification on pages 13-22 discloses that brazil nut 2S albumin which has been reduced and alkylated induces decreased amounts of IgE antibodies in rats sensitized orally and by intraperitoneal injection.

The specification does not disclose any methods whereby reduced and alkylated food allergens may be used to treat food allergy in vivo. The specification merely discloses in the examples that reduced and alkylated Ber e 1 induces decreases sensitivity as measured by IgE production against the protein as compared to natural Ber e 1 in rats.

The specification has not adequately disclosed a method for treating "food allergy" using any "modified food allergens." Absent a limiting definition in the specification, the term "food" encompasses all things that can be eaten for energy. Therefore, any carbohydrate, protein or lipid molecules are encompassed by the term "food allergen." The specification has not adequately disclosed a method for treating allergy to any carbohydrate, protein or lipid molecules which have been reduced and alkylated. Such a recitation encompasses a genus of methods that would require an undue amount of experimentation to practice the invention commensurate in scope with the claims. In addition, since there is no limiting definition in the specification for what is encompassed by "food allergy," it would seem that any person having IgE antibodies to any protein that may be eaten is encompassed by the instant claim recitation. Such a recitation includes asthma, which can be caused by ovalbumin which is both any protein that can be eaten and an allergenic protein of food, yet the specification has not adequately described a method of treating asthmatic patients. As such, one of ordinary skill in the art would be required to perform undue experimentation to practice the invention commensurate in scope with the claims.

The specification does not adequately disclose a method for treating an individual suffering from or having a tendency to develop a food allergy comprising administering a food

allergen that has been alkylated and reduced. The art recognizes that antibody-antigen binding is highly unpredictable. Given that the specification teaches that reduction and alykylation alters the conformational structure of the food allergens, it is highly unpredictable as to whether antibody binding will be increased of decreased after such modification. In some instances, denatured proteins with altered conformation exhibit increased IgE binding, not decreased IgE binding. For example, in Maleki et al. teaches that denaturation of peanut proteins by roasting increases binding to serum IgE from allergic individuals at approximately 90 fold higher levels than undenatured peanuts. (PTO-892, Reference U; In particular, page 767 first paragraph of discussion). But, even when the modified food allergen does exhibit reduced IgE binding, whether that protein can be used therapeutically to treat food allergies is still unpredictable because those modified proteins are not necessarily able to induce the requisite immune responses necessary to promote tolerance. For example, the art of Peng et al. (PTO-892; Reference V) teaches that denatured ovalbumin does not induce oral tolerance because the molecules are hypoallergenic and have decreased sensitizing capacity (In particular, page 478 paragraph spanning columns, abstract, whole document). Therefore, it is highly unpredictable whether any particular modified food allergen will downregulate the production of IgE, induce production of Thelper-1 IgG antibodies and be enabled for therapeutic use to treat food allergies. The specification has not adequately disclosed a genus of methods of treating food allergy using any reduced and alkylated food allergen, any "2S albumin, any lipid transfer protein, any conglutin, or any plant storage protein as encompassed by the instant claims. As such, the method would be unpredictable and would require one of ordinary skill in the art to perform undue experimentation to practice the invention commensurate in scope with the claims.

The specification has not adequately disclosed a method of treating allergy by administering a modified food allergen "in a dosage form chosen selected from the group consisting of a capsule, tablet, lozenge, dragee, pill, droplets, suppository, aerosol, powder, spray, vaccine, ointment, paste, cream, inhalant, or and patch" "orally, intraperitoneally, subcutaneously, intravenously, intramuscularly, pulmonarily, or via mucosa." The specification never demonstrates that modified Ber e 1 can be used to treat food allergy in any manner. The specification does not adequately provide support for the ability of the modified Ber e 1 allergen to be administered in the recited dosage forms and delivered by the recited dosage routes. The art shows that the dosage method employed plays a substantial role in the ability of such a protein to be able to treat allergies. As such, one of ordinary skill in the art would be required to perform undue experimentation to treat any food allergy using any modified food allergen in any dosage form given by any dosage route. As stated above, the art of Peng et al. shows that food allergens with altered conformation cannot induce tolerance when administered orally in vivo (In particular, page 478 paragraph spanning columns, abstract, whole document). Of particular note is that it is especially unpredictable how food allergies may be treated by administration of the modified food allergen pulmonarily. Given the lack of examples in the specification and detailed disclosure and guidance on how to make any use the genus of modified food allergens to treat any "food allergy," one of ordinary skill in the art would be required to perform undue experimentation to practice the invention commensurate in scope with the claims.

Substantiating evidence may be in the form of animal tests, which constitute recognized

screening procedures with clear relevance to efficacy in humans. See Ex parte Krepelka, 231 USPQ 746 (Board of Patent Appeals and Interferences 1986) and cases cited therein. Ex parte Maas, 9 USPQ2d 1746.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

9. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: a method of decreasing the allergenicity of 2S albumin Ber e 1 from brazil nuts by alkylating and reducing the protein.

Applicant is not in possession of: a method for treating an individual suffering from or having a tendency to develop **a food allergy** comprising administering to said individual a therapeutically effective amount of **a modified food allergen**, wherein **the food allergen** is modified by reduction and alkylation of claim 1; wherein **the food allergen** is **an allergenic food protein** of claim 2; wherein **the food allergen** is **a seed plant storage protein** of claim 3;

wherein **the plant storage protein** is **a 2S albumin, lipid transfer protein (LTP), or conglutin** of claim 4; the **plant storage protein** is **a tree nut or a 2S albumin** of claim 5; wherein **the plant storage protein** is **brazil nut 2S albumin** of claim 6; wherein administering **the modified food allergen** induces production of Thelper-1 mediated subclasses of IgG antibodies of claim 12; and wherein administering **the modified food allergen** results in down regulating the production of IgE antibodies of claim 13 and as applied to claims 7-11.

The skilled artisan cannot envision all the contemplated method possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey

with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-13 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/074250 (IDS filed on 08/22/2006).

WO 02/074250 teaches a method for treating an individual suffering from food allergy comprising administering to said individual a therapeutically effective amount of a protein food allergen modified by reduction and alkylation (In particular, page 3, line 24 to page 4, line 30,

page 40, lines 1-29, claims, whole document); wherein the food allergen is a plant storage protein (In particular, Appendix 8); wherein the plant storage protein is a 2S albumin, lipid transfer protein (LTP) or conglutin (In particular, Appendix 8); wherein the plant storage protein is a tree nut or seed a 2S albumin (In particular, Appendix 8); wherein the plant storage protein is brazil nut 2S albumin (In particular, Appendix 8, page 176); wherein said reduction uses a reducing agent selected from the group consisting of 2-mercaptoethanol, dithiothreitol, dithioerythritol, and tributylphosphine (In particular, page 32, line 5-21); said alkylation uses an alkylating agent chosen selected from the group consisting of N-ethylmalimide, cystamine, iodoacetamide, and iodoacetic acid (In particular, page 32, lines 5-21); in a dosage form chosen selected from the group consisting of a capsule, tablet, lozenge, pill, droplets, suppository, aerosol, powder, spray, vaccine, ointment, paste, cream, inhalant, or and patch(In particular, page 4 lines 19-23; page 42, line 21 to page 43, line 28); wherein the dosage form further comprises a pharmaceutically acceptable carrier and/or an adjuvant (In particular, page 34 line 5 to page 36, line 25); wherein said administering is effected orally, intraperitoneally, subcutaneously, intravenously, intramuscularly, or mucosa (In particular, page 4 lines 19-23; page 42, line 21 to page 43, line 28); wherein administering the modified food allergen induces production of Thelper-1 mediated subclasses of IgG antibodies (In particular, page 3, line 24 to page 4, line 30, page 40, lines 1-29, whole document); and wherein administering the modified food allergen results in down regulating the production of IgE antibodies (In particular, page 3, line 24 to page 4, line 30, page 40, lines 1-29, whole document).

The reference teachings anticipate the claimed invention.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

December 21, 2009

Nora M. Rooney

Patent Examiner

Technology Center 1600

/Nora M Rooney/

Examiner, Art Unit 1644